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Different perceptions of the burden of upper GI endoscopy: an empirical study in three patient groups

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Abstract

Background Few studies have evaluated patients' perceived burden of cancer surveillance tests. Cancer screening and surveillance, however, require a large number of patients to undergo potentially burdensome tests with only some experiencing health gains from it. We investigated the determinants of patients' reported burden of upper gastrointestinal (GI) endoscopy by comparing data from three patient groups.

Patients and methods A total of 476 patients were included: 180 patients under regular surveillance for

Barrett esophagus (BE), a premalignant disorder; 214 patients with non-specific upper GI symptoms (NS), and 82 patients recently diagnosed with upper GI cancer (CA). We assessed pain, discomfort and overall burden experienced during endoscopy, symptoms in the week afterwards and psychological distress over time (Hospital Anxiety and Depression scale and Impact of Event Scale).

Results Two-thirds (66%) of patients reported discomfort and overall burden of upper GI endoscopy. Only 23% reported any pain. BE patients reported significantly less discomfort, pain and overall burden than the other patients: those with NS reported more discomfort, CA patients more pain, and both more overall burden. These differences could be statistically explained by the number of previous endoscopies and whether sedation was provided or not, but not by patient characteristics.

Conclusion The perception of upper GI endoscopy varies by patient group, due to potential adaptation after multiple endoscopies and aspects of the procedure.

Keywords Upper gastrointestinal endoscopy · Endoscopic surveillance · Barrett esophagus · Perceived patient burden · Discomfort · Anxiety · Distress

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Introduction

Opportunities for screening and surveillance of premalignant conditions have increased and will increase in the future. However, such interventions can be burdensome, and, as in any screening situation, the number of subjects exposed to this burden is often much higher than the number of subjects experiencing the beneficial health effects of the screening [1].

Upper gastrointestinal (GI) endoscopy is commonly used to diagnose and treat patients with a range of conditions and symptoms. Complications related to upper GI endoscopy are rare, and it is considered to be a safe procedure [2, 3]. Patients with Barrett esophagus (BE), a premalignant condition mostly without physical symptoms but associated with an increased risk of developing esophageal adenocarcinoma of 0.5% per year, are recommended to undergo regular biennial endoscopic surveillance for early detection of esophageal cancer [4]. All patients participating in surveillance experience the pain and discomfort of biennial upper GI endoscopy, whereas progression to adenocarcinoma occurs only in a minority of BE patients [5–8] and undisputable evidence that surveillance prolongs survival is still lacking [9–12]. Hence, the patients' perceived burden of upper GI endoscopy testing needs to be taken in to account in evaluating the health benefits of surveillance of subjects with BE.

In some situations, there is a trade-off between the effectiveness of screening (or surveillance) and the test uptake. For example, colorectal cancer screening using sigmoidoscopy is more effective than faecal occult blood testing [13]. At present, this trade-off is not relevant for surveillance of BE because a less burdensome test than upper GI endoscopy is not available, but the recognition that upper GI endoscopy is burdensome may prompt a reconsideration of the frequency of surveillance. Ongoing studies aim to identify groups of BE patients at lower risk of developing esophageal cancer than others, so that offering less frequent surveillance may be warranted [14].

At the patient level, empirical data on perceived burden of upper GI endoscopy can be used in the process of informing subjects with BE who consider participation to a surveillance programme. In a general sense, empirical data of the patients' perceived burden of testing may contribute to subjects' informed decision-making on participation (or non-participation) to screening or surveillance and hence, to quality of health care [15].

Studying the determinants of patients' perceived burden of upper GI endoscopy, e.g. by comparing data from different patient groups, may allow for the identification of patient groups who are likely to experience more pain or discomfort than others. This information can be used in practice guidelines, e.g. on provision of sedation to prevent pain and discomfort, or other types of patient support. Studying determinants of patients' perceived burden is of additional interest from the perspective of evaluation research. If patients' perception of the burden of endoscopy differs by the context of e.g., surveillance or diagnostic work-up, the generalisability of data from one context to another is limited.

Our previous work [16] has shown that BE patients under regular surveillance perceive upper GI endoscopy as

burdensome. They experienced anxiety and discomfort, but hardly reported pain or symptoms. We analysed potential determinants of the perceived burden of upper GI endoscopy by comparing BE patients with two additional patient groups, i.e., patients with non-specific upper GI symptoms (NS) and patients with a recent diagnosis of cancer of the upper GI tract (CA).

Methods

Ethics approval

The Medical Ethical Review Board of Erasmus MC—University Medical Center Rotterdam, The Netherlands, approved of the study (MEC 03.1064; October 9, 2003).

Patients

- Patients undergoing upper GI endoscopy for surveillance of BE were participants of an ongoing trial (CYBAR), whose endoscopic burden was previously reported [16]. Inclusion criteria were: BE segment of 2 cm or more confirmed by a histological diagnosis of intestinal metaplasia, absence of high-grade dysplasia and carcinoma, willingness to adhere to endoscopic surveillance, ability to read the Dutch language and informed consent.
- Patients with non-specific upper GI symptoms (NS) were referred for endoscopy by their respective GPs because of non-specific upper GI symptoms. They needed to be able to read the Dutch language, provide informed consent, not to have “alarm symptoms” such as hematemesis, melena, or dysphagia, and not be diagnosed with BE previously.
- Patients with a recent diagnosis of upper GI cancer (CA) were referred for upper GI endoscopy *plus* ultrasonography (EUS) to determine therapeutic options. Ability to read the Dutch language and to give informed consent was also required in these patients. Patients were recruited from one academic and two regional hospitals for BE, two regional hospitals for NS and in one academic hospital for CA.

Endoscopic procedure

BE and NS patients underwent endoscopy with adult endoscopes (Olympus GIF-Q160, Zoeterwoude, The Netherlands). In the group of cancer patients, a combined endoscopy and EUS was performed with a Olympus GF-UM160. More than 95% of patients received oral anaesthetics (Xylocain 10% spray, Astra Zeneca, Zoetermeer,

The Netherlands) preceding the introduction of the endoscope. Additional sedation with 2,5–5 mg midazolam (Roche, Woerden, The Netherlands) intravenously was offered as a standard procedure to all cancer patients, but was only administered with explicit patient consent. In BE and NS patients this was not standard, but it was administered on a patient's request. Practice variations between and within countries in the use of sedation for upper GI endoscopy are common [17].

Hypotheses

Perceived burden of endoscopy was operationalised as pain and discomfort during the procedure, symptoms afterwards and psychological distress over time. We hypothesized that subjects who had previous endoscopies may get used to it to some extent and hence report less burden. Demographic characteristics (age, sex, educational level, employment status, etc) were considered as potential confounders. We expected that BE patients may get used to regular endoscopy to some extent, and that they adhere to surveillance expecting that the test result will be reassuring. Therefore, we expected BE patients to report less discomfort and burden than the patients with non-specific GI symptoms, who had less endoscopy experience. We also expected the BE group to report less burden from the endoscopy than the cancer patients, due to the endoscopy itself (combined with EUS in the cancer patients) and the fact that cancer patients were aware of their generally bad prognosis. Table 1 shows the potential determinants of perceived burden of endoscopy between patient groups.

Questionnaires and measurements

Patients were asked to complete questionnaires at different time points, i.e., one week before the endoscopy (baseline), at the day of endoscopy (just before undergoing it), one week and one month after endoscopy [16]. In order to minimize the questionnaire load for CA patients they received only two questionnaires: the first on the day of endoscopy and the other one week afterwards. Some baseline items had to be included in the 'endoscopy day' questionnaire in the CA group. The content of the questionnaires is described below.

Pain and discomfort

Separate items in the questionnaire one week after endoscopy were used to assess pain and discomfort, respectively, as experienced during the procedure, for four steps of the procedure: the introduction of the endoscope, the endoscopy itself, the removal of the endoscope, and the period directly after endoscopy. Subjects were offered three

Table 1 Potential determinants of perceived burden of endoscopy for three patient groups

Determinant	BE	NS	CA
Indication for endoscopy	Regular endoscopic surveillance for early detection of cancer	To find out if symptoms can be explained by e.g. a hiatal hernia or duodenal ulcer; a life-threatening diagnosis is not expected.	To determine whether intentionally curative therapy is possible or not
Endoscopy experience	Yes, under endoscopic surveillance	Limited, ranging from 0 to some	Yes (by definition: at least one previous endoscopy needed to diagnose the cancer)
Generic health status	Generally healthy	Mild impairment (aspecific gastrointestinal symptoms)	Seriously impaired (cancer diagnosis)
Age	In-between	Youngest	Older
Sex	More males than females	Equal sex distribution	Predominantly male
Endoscopy procedure	Normal endoscopy procedure, sedation only on patient request	Normal endoscopy procedure, sedation only on patient request	Endoscopy combined with ultrasonography; sedation routinely offered

response options ('no', 'quite' and 'very' painful or discomforting, respectively). Additionally, patients rated the overall burden of undergoing the endoscopy (very, somewhat, not burdensome) [16].

Symptoms

We compared the prevalence of 10 symptoms experienced in the week after endoscopy with the prevalence at baseline. For CA patients, the baseline questions were asked at the day of endoscopy. Presence of throat ache, heartburn, regurgitation, flatulence or feeling bloated, vomiting, hematemesis, dysphagia for solid foods or for of liquids, diarrhea, and constipation, was assessed using four response options (not at all, one day, 2–3 days, 4 or more days) [16].

Psychological distress (BE and NS patients)

We assessed general distress using the Hospital Anxiety and Depression scale (HAD) at all time points [18, 19]. Anxiety and depression scores of this scale range from 0–21, with scores of 11 or over indicating clinical, and scores between 8 and 10 indicating borderline anxiety or depression [18, 19]. We analysed the pattern of scores across measurements, assuming scores to return to normal after endoscopy. Scores from a Dutch general population sample ($n = 1901$; mean age = 61 year; 51% female) were available for comparison [19].

At baseline and at one week we also measured specific distress with the Impact of Event Scale (IES) [20, 21]. At baseline we assessed intrusive and avoiding thoughts regarding the endoscopy itself, and at one week regarding the communication of the final test result. The total scale ranges between 0 and 75, with scores of 26 or over indicating a high risk of developing a stress disorder [22].

Psychological distress (CA patients)

For CA patients we omitted the HAD and the IES measures regarding the endoscopy itself, because we expected that distress in these patients was already at the top of the scale, making any additional distress caused by the procedure itself indiscernible. The IES to assess specific distress regarding the endoscopy result was included in the questionnaire at the day of endoscopy, because these patients received the endoscopy results earlier than the next questionnaire.

Demographics and other data

Demographic data were collected at baseline (at the endoscopy day for CA patients). The EQ-5D self-classifier results in a patient's classification of own health on five

domains: mobility, self-care, usual activities, pain, and anxiety and depression (3 response options: no, some, severe/ complete limitations) and a summary score [23–25]. We asked BE and NS patients whether this was their first, second or a later endoscopy. Whether sedation was used during endoscopy was recorded separately.

Analyses

Differences in demographic and treatment characteristics between patient groups were analysed by Chi-square tests for categorical variables or one-way analysis of variance (ANOVA) for continuous variables.

The items for pain and discomfort were combined into summary scores to enable adjustment for confounders and analysis of determinants, by adding up the item responses (0, 1, 2, respectively) of the 4 items (range of pain and discomfort summary scores: 0 (no pain or discomfort) to 8) [16]. The response to the single item rating of overall burden was also treated as a summary score, with a range from 0 (no burden) to two [16]. Because these summary scores had a limited number of possible values and because the data were not distributed normally, we chose to analyse them with proportional odds models [26]. These models produce odds-ratios (ORs) for cumulative probabilities of the outcome variables. Proportional odds models are a variant of simple logistic regressions, but now ORs for dichotomies at all possible cut-off levels are estimated. E.g., for a variable with three possible outcomes 1, 2, and 3, ORs are estimated for (1 + 2) vs. 3 and for 1 vs. (2 + 3). The OR presented represents an overall OR, that is assumed to be similar across cut-off levels. Because some of the outcome variables and determinants had 10–15% missing data, and there were no reasons for selective missing data, we used multiple imputation (function *AreImpute* in *Splus* 6.0) [27] so that all available information in our dataset was used. In multivariate analysis of the determinants of patients' perceived burden with the proportional odds model, we first adjusted for confounders (age, sex and employment status). Subsequently we evaluated the potential effects of the following determinants on discomfort, pain and overall burden, respectively:

- patient group (BE, NS or CA). This variable combines the differences in the endoscopy procedure (with or without EUS, sedation) and the indication to undergo the endoscopy. For BE and NS patients, this analysis was refined by additional separate analysis of the effect of the number of previous endoscopies (continuous, truncated at ≥ 20).
- baseline generic health status (EQ 5D summary score).
- whether sedation was administrated or not.
- baseline HAD anxiety score (not available for the CA patients).

The prevalence of symptoms before and after endoscopy was compared using a method analogous to the Wilcoxon test. Responses were ranked and ANOVA was applied to the differences in these ranks [16].

The continuous HAD and IES scores were compared over time in SAS version 8.2 with repeated-measures ANOVA, using 'Proc Mixed' with REML and a compound symmetry covariance structure. Models comprised main effects of time (the measurements), confounders, determinants and interactions between determinants and time.

Proportional odds models were estimated with Splus 6.0. All other analyses were conducted in SPSS version 11.0.1.

Results

Patients and response

In total, 684 patients were eligible for inclusion: 192 BE, 365 NS and 127 CA patients. The overall response rate was 70% with 476 patients completed at least one questionnaire. The response differed by patient group; it was 180/192 (94%) in BE patients, 214/365 (59%) in NS patients and 82/127 (65%) in CA patients. Most BE patient had no dysplasia (78%), 22% had low-grade dysplasia [16]. NS patients were diagnosed with hiatal hernia (45%), non-specific gastritis (25%), reflux esophagitis (20%) and some other diagnoses (e.g. ulcer, polyps; 10%). CA patients underwent endoscopy and EUS for staging of esophageal carcinoma (72%), gastric cancer (26%) or lymphoma (2%).

Differences between groups in mean age, sex and employment status were statistically significant ($P < 0.001$) (Table 2). We therefore considered these variables as confounders and controlled for them in further analyses.

About 84% of the BE patients had had two or more previous endoscopies [16], compared with 18% of the NS patients ($P < 0.001$). Seventy-seven per cent of the CA patients received sedation during endoscopy, compared with 27% of the BE and 9% of the NS patients ($P < 0.001$). The differences in the mean EQ-5D summary score were in the expected direction ($P < 0.001$) (Table 2).

Pain and discomfort

Tables 3–5 show that the patient groups differed significantly in reported discomfort, pain and overall burden of endoscopy. The p-values shown for the summary scores relate to univariate analysis of differences between the patient groups before adjustment for confounders.

Table 6 shows these adjusted differences in summary scores for pair wise comparisons between the groups, and

how these are affected by the determinants. NS patients reported significantly more discomfort than BE patients, as demonstrated by the significant OR of 1.69. After adjusting for differences in the number of previous endoscopies, the difference in reported discomfort between NS and BE patients was no longer significant. Similarly, the difference in reported discomfort between NS and BE patients could also be explained by differences regarding the administration of sedation. The differences between the NS and BE groups in the baseline EQ-5D summary score and in baseline anxiety scores did not explain the differences in reported discomfort: the ORs remained significant. Reported pain during upper GI endoscopy did not differ between NS and BE groups. The difference in reported overall burden was significant (OR = 1.64, $P = 0.03$). This difference became also insignificant after adjustment for the number of previous endoscopies and for sedation.

CA patients reported significantly more pain (OR = 2.69, $P < 0.01$) and overall burden than BE patients (OR = 2.37, $P < 0.01$; Table 6). The differences in reported pain could not be explained by differences in baseline EQ-5D summary scores or whether sedation had been administered or not (all ORs remained significant, Table 6). CA and BE patients did not differ in reported discomfort (OR = 1.22, $P = 0.42$), but after taking differences in the provision of sedation into account, the difference in reported discomfort became significant (OR = 2.06, $P = 0.01$).

Symptoms

After endoscopy, throat ache was the only symptom that was reported more often than before the procedure (51 vs. 23%; $P < 0.001$). Other symptoms did not increase in frequency. Compared to BE patients, the increase in throat ache was smaller for NS patients and larger for CA patients ($P < 0.001$); 31% of NS patients reported throat ache before and 46% afterwards, compared to 12% and 47% of BE patients, and 12% and 70% of CA patients, respectively.

Psychological distress

Figure 1 shows unadjusted mean anxiety and depression scores (HAD—not available for CA patients) by patient group over time.

After adjusting for confounders (repeated measures ANOVA), anxiety levels were similar between the BE and NS groups across measurements, but the pattern differed significantly between them (interaction effect of 'group' with 'time', $P = 0.01$): BE patients reported lower anxiety levels at the start and slightly higher at the end. Determinants (number of previous endoscopies, baseline EQ-5D summary score, sedation) did not influence this pattern of

Table 2 Patient characteristics^a

	BE	NS	CA	Differ ^b	N
Group	180	214	82	N.A.	476
Mean age (sd)	62 (12)	54 (16)	64 (10)	<0.001	474
Sex: male	119 (66%)	101 (47%)	66 (80%)	<0.001	476
Employment					
Paid employment	59 (34%)	85 (44%)	25 (36%)	<0.001	438
Retired	87 (50%)	65 (34%)	38 (54%)		
Unpaid/unemployed	29 (17%)	43 (22%)	7 (10%)		
Civil status					
Married/ together	134 (77%)	137 (69%)	57 (80%)	0.034	444
Never married/ tog.	13 (7%)	26 (13%)	3 (4%)		
Divorced	10 (6%)	23 (12%)	4 (6%)		
Widowed	18 (10%)	12 (6%)	7 (10%)		
Education					
Primary	35 (20%)	37 (19%)	16 (23%)	0.498	435
Secondary	95 (56%)	122 (63%)	43 (61%)		
Tertiary	40 (24%)	35 (18%)	12 (17%)		
Hospital					
Academic center (1)	37 (21%)	0	82 (100%)	N.A.	476
Regional hospital (3)	143 (79%)	214 (100%)	0		
Sedation: yes	43 (27%)	18 (9%)	56 (77%)	<0.001	419
Endoscopy number					
First	1 (1%)	99 (59%)	Unknown	<0.001	338
Second	26 (15%)	38 (23%)			
Third or later	144 (84%)	30 (18%)			
EQ-5D summary score	0.85 (0.18)	0.73 (0.22)	0.77 (0.21)	<0.001	433

N.A., Not assessed

^a Data for the BE group were published previously [16]^b χ^2 -test (categorical variables) or *F*-test (continuous) for differences between patient-groups

anxiety over time (no significant interaction effects with ‘time’). Anxiety scores of both NS and BE patients were significantly higher at all time points than reported by a general population sample (score = 3.9; $P < 0.001$ for each group at each measurement) [19].

At all measurements, depression scores were lower in BE than in NS patients ($P < 0.001$). This difference was significantly larger before than after endoscopy (interaction effect of ‘group’ with ‘time’, $P = 0.01$). The number of previous endoscopies affected the pattern of depression over time (interaction effect of ‘number of previous endoscopies’ with ‘time’ $P = 0.046$) making the pattern of the two groups more similar. Depression scores differed from those reported by the general population sample: BE patients reported significantly lower levels at all measurements, while baseline NS scores were significantly higher (norm score = 3.7, $P < 0.001$ for each comparison).

Specific distress (IES) scores regarding the endoscopy itself and its outcome were lower in BE patients than in NS patients (mean scores at baseline measurement and 1 week measurements are BE 5.5 (sd 9.5), NS 12.9 (sd 14.7), and BE 3.5 (sd 7.7), NS 9.4 (sd 14.3) respectively, $P < 0.001$). The determinants did not affect this difference. In both BE and NS patients, specific distress regarding the endoscopy

(IES, baseline measurement) was higher than regarding the test result (IES, one week measurement) ($P < 0.001$). High IES-distress scores regarding the endoscopy were seen in 51 patients (14%). CA patients (mean IES score 22.3 (sd 17.8)) had significantly higher distress levels (IES) regarding the test-result than the other patient groups ($P < 0.001$).

Discussion

This study is the first to investigate determinants of patients’ perceived burden of upper GI endoscopy. Patients undergoing endoscopy for different reasons reported a different burden from the procedure. BE patients who underwent endoscopy as part of regular surveillance, reported the lowest discomfort, pain and overall burden, confirming our hypotheses in this respect. Patients with non-specific GI complaints reported more discomfort from the procedure, while those diagnosed with cancer experienced more pain and both groups reported more overall burden than patients under surveillance for BE. These differences remained significant after adjustment for confounders (age, sex, employment status). Differences in

Table 3 Discomfort during upper GI endoscopy as reported by patients^a

Discomfort	Not	Quite	Very	<i>n</i>	Differ ^b
Introducing the endoscope	141 (34%)	177 (42%)	99 (24%)	417	$P < 0.001$
NS	42 (24%)	76 (43%)	58 (33%)	176	
BE	64 (37%)	81 (47%)	27 (16%)	172	
CA	35 (51%)	20 (29%)	14 (20%)	69	
Undergoing endoscopy	166 (40%)	162 (39%)	89 (21%)	417	$P = 0.024$
NS	62 (35%)	63 (36%)	51 (29%)	176	
BE	75 (44%)	72 (42%)	25 (15%)	172	
CA	29 (42%)	27 (39%)	13 (19%)	69	
Removing the endoscope	290 (70%)	90 (22%)	35 (8%)	415	$P < 0.001$
NS	97 (55%)	52 (30%)	26 (15%)	175	
BE	144 (84%)	24 (14%)	3 (2%)	171	
CA	49 (71%)	14 (20%)	6 (9%)	69	
Period immediately after	317 (78%)	71 (17%)	20 (5%)	408	$P = 0.348$
NS	132 (77%)	29 (17%)	11 (6%)	172	
BE	136 (81%)	29 (17%)	4 (2%)	169	
CA	49 (73%)	13 (19%)	5 (8%)	67	
Discomfort summary score (range: 0–8)	Mean (sd)				
All	2.35 (2.10)			406	$P < 0.001$
NS	2.92 (2.36)			171	
BE	1.88 (1.69)			168	
CA	2.07 (1.99)			67	

^a Data for the BE group were published previously [16]

^b Significance of differences between three groups as determined by Chi-square test (categorical variables) or proportional odds models for ordinal response data (summary score). No correction for confounders

Table 4 Pain during upper GI endoscopy as reported by patients^a

Pain	Not	Quite	Very	<i>n</i>	Differ ^b
Introducing the endoscope	332 (80%)	68 (16%)	17 (4%)	417	$P = 0.050$
NS	135 (77%)	29 (17%)	12 (7%)	176	
BE	145 (85%)	24 (14%)	2 (1%)	171	
CA	52 (74%)	15 (21%)	3 (4%)	70	
Undergoing endoscopy	320 (77%)	77 (19%)	17 (4%)	414	$P < 0.001$
NS	141 (81%)	23 (13%)	10 (6%)	174	
BE	137 (81%)	28 (17%)	5 (3%)	170	
CA	42 (60%)	26 (37%)	2 (3%)	70	
Removing the endoscope	365 (88%)	39 (9%)	11 (3%)	415	$P = 0.098$
NS	152 (87%)	16 (9%)	6 (3%)	174	
BE	157 (92%)	11 (6%)	3 (2%)	171	
CA	56 (80%)	12 (17%)	2 (3%)	70	$P = 0.454$
Period immediately after	350 (84%)	52 (13%)	15 (4%)	417	
NS	147 (84%)	23 (13%)	6 (3%)	176	
BE	145 (85%)	22 (13%)	4 (2%)	171	
CA	58 (83%)	7 (10%)	5 (7%)	70	
Pain summary score (range: 0–8)	Mean (sd)				
All	0.86 (1.60)			413	$P = 0.02$
NS	0.91 (1.81)			173	
BE	0.66 (1.35)			170	
CA	1.20 (1.60)			70	

^a Data for the BE group were published previously [16]

^b Significance of differences between three groups as determined by Chi-square test (categorical variables) or proportional odds models for ordinal response data (summary score). No correction for confounders

Table 5 Overall burden of upper GI endoscopy as reported by patients^a

Overall burden	Not	Quite	Very	<i>n</i>	Differ ^b
Endoscopy in general	137 (34%)	204 (51%)	58 (15%)	399	<i>P</i> = 0.007
NS	48 (30%)	82 (50%)	32 (20%)	162	
BE	68 (41%)	87 (52%)	12 (7%)	167	
CA	21 (30%)	35 (50%)	14 (20%)	70	
Overall burden summary score (range: 0–2)	Mean (sd)				
All	0.80 (0.67)				399
NS	0.90 (0.70)				162
BE	0.67 (0.61)				167
CA	0.90 (0.71)				70

^a Data for the BE group were published previously [16]

^b Significance of differences between three groups as determined by Chi-square test (categorical variable) or proportional odds models for ordinal response data (summary score). No correction for confounders

Table 6 Differences in discomfort summary score, pain summary score and overall burden score, pair wise between patient groups (after correction for age, sex and employment status as confounders); and effects of other determinants than patient group on these differences

Determinant	Discomfort score			Pain score			Overall burden		
	OR ^a	95% CI ^b	<i>P</i> -value	OR ^a	95% CI ^b	<i>P</i> -value	OR ^a	95% CI ^b	<i>P</i> -value
NS compared to BE (BE = reference group)									
Patient group: NS versus BE	1.69	1.15–2.47	< 0.01	1.09	0.70–1.71	0.70	1.64	1.05–2.55	0.03
+ Number of previous endoscopies	1.49	0.98–2.27	0.06	1.19	0.73–1.94	0.50	1.56	0.96–2.53	0.07
+ Baseline EQ–5D	1.51	1.02–2.23	0.04	0.83	0.53–1.32	0.44	1.49	0.96–2.33	0.08
+ Baseline anxiety	1.63	1.12–2.39	0.01	1.04	0.66–1.64	0.86	1.59	1.02–2.49	0.04
+ Sedation	1.42	0.96–2.09	0.08	1.08	0.68–1.72	0.73	1.40	0.88–2.22	0.15
CA compared to BE (BE = reference group) ^c									
Patient group: CA versus BE	1.22	0.75–1.99	0.42	2.69	1.51–4.77	<0.01	2.37	1.38–4.07	<0.01
+ Baseline EQ–5D	1.07	0.66–1.74	0.79	2.32	1.29–4.18	<0.01	2.10	1.21–3.66	<0.01
+ Sedation	2.06	1.16–3.64	0.01	2.71	1.40–5.27	<0.01	3.10	1.68–5.74	<0.01

^a Odds ratios were calculated by proportional odds models for ordinal response data. They show the differences between the patient groups, corrected for confounders and the determinant mentioned

^b 95% confidence interval

^c Numbers of previous endoscopies and baseline anxiety were not available for CA patients

baseline anxiety scores or in baseline general health (EQ–5D) did not explain the differences in reported discomfort or pain. Differences in the number of previous endoscopies, and in whether sedation was provided during endoscopy or not, explained part of the differences in reported discomfort between NS and BE patients. Whether sedation was provided or not did not explain the differences in reported pain and overall burden between BE and CA patients.

The study also confirms that that upper GI endoscopy is burdensome for all groups of patients: two-thirds of the total group of patients reported discomfort and overall burden from the procedure, and patients were distressed beforehand. These results may however underestimate the actual burden because this empirical study was limited to patients who actually underwent upper GI endoscopy, hence excluding patients who refrained from undergoing endoscopy because of past or anticipated adverse experiences. Another potential limi-

tation of our study results from the differences in response rates between the groups.

Differences between patient groups were also found for symptoms resulting from the endoscopy. Of all symptoms explored, only throat ache increased after upper GI endoscopy. CA patients reported a higher increase in throat ache than BE patients and NS patients. As upper GI endoscopy hardly caused any symptoms, we considered an investigation into determinants of these differences to be less interesting and therefore omitted those analyses.

Furthermore, BE and NS patients differed in the levels of generic (HAD) and specific (IES) distress they reported. Specific distress (IES) was significantly higher in NS patients than in BE patients, both regarding the endoscopy itself and its result. General distress (HAD) also differed between groups: BE patients reported less depression across all measurements and the pattern of anxiety and depression across measurements was different. However,

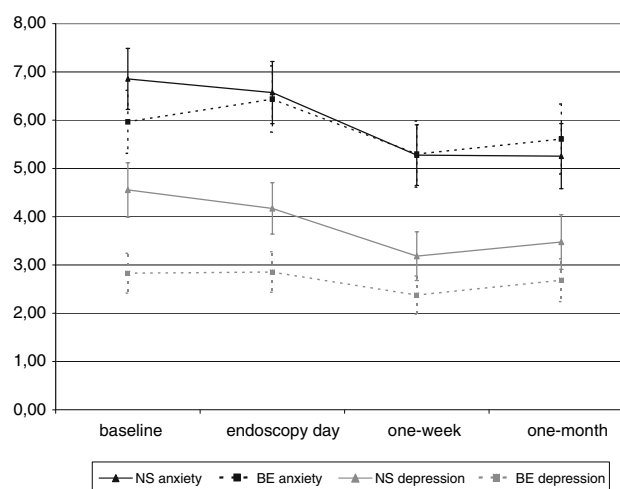


Fig. 1 Differences between BE and NS groups in Hospital Anxiety and Depression (HAD) scale scores for general distress before and after upper GI endoscopy (mean scores, no adjustment for confounders)

general distress is not necessarily related to the endoscopy. The persistent higher depression scores across different time points suggest that NS patients have more depressive symptoms in general but that this was not related to the endoscopy. The different pattern of anxiety levels before and after endoscopy, however, suggests that the patient groups also differed in endoscopy-related distress. The pattern corroborated the findings of the specific (IES) distress scores: NS patients were more distressed than BE patients before the endoscopy. The investigated determinants did not explain the differences between groups in specific distress or general distress pattern, except for the number of previous endoscopies explaining part of the difference in the depression scores.

BE patients thus reported less distress and also less pain or discomfort than other patient groups. This was not caused by differences in patient characteristics (age, sex, employment status, baseline anxiety, baseline general health). There are several potential reasons why the reported burden differs. Firstly, BE patients are under regular surveillance and may get used to or adapt to the procedure decreasing its burden. As the number of previous endoscopies explained the lower distress, discomfort and overall burden reported in the BE group, we conclude that getting used, or adapting to endoscopy plays a role.

Secondly, patients who perceive a greater benefit of the test may weigh its burden differently and consequently report less burden. BE patients potentially have more to gain from early discovery of adenocarcinoma than NS patients, who are usually referred for endoscopy to detect potential explanations for their symptoms, and also more than CA patients for whom endoscopy and ultrasonography are only part of the procedure to determine their treatment

options and prognosis. As we did not measure perceived expected benefit of the endoscopy we are not able to determine whether this mechanism is part of the explanation.

Thirdly, the endoscopic procedure was slightly different for the different patient groups. CA patients received sedation more often. Adjusting for this difference into the analysis did not explain the differences in pain and overall burden, whereas the difference in reported discomfort became significant after adjustment for sedation. These results suggest that differences in the proportions of patients receiving sedation during endoscopy did not explain the differences between the groups, and that sedation was provided to those patients who really needed it. The procedure for CA patients also differed; they underwent upper GI endoscopy combined with ultrasonography, and for the combined procedure an endoscope with a slightly larger diameter is used. Our data did not allow us to test separately whether this affected perceived pain and overall burden. Finally, most CA patients had esophageal carcinoma, and this disease may make passing the endoscope through the esophagus more difficult and therefore more painful.

We measured general psychological distress (HAD) at different time points; assuming that a pattern of higher distress levels before compared to after endoscopy indicates that the procedure causes distress. As discussed in a previous paper [16], this may be debated for the reason that lower distress levels afterwards may also result from a reassurance effect of patients receiving a negative test result (no serious disease present). Nevertheless, the fact that the specific distress (IES) score relating to the endoscopy was higher than the IES score relating to the test outcome led us to conclude that the prospect of undergoing upper GI endoscopy does indeed increase distress levels.

Even if upper GI endoscopy causes HAD anxiety and depression scores to be increased before the endoscopy, the relevance of these increased distress levels can be questioned. Anxiety may be a relevant problem with 20% of patients having scores indicating clinical anxiety levels at baseline, while the depression scores are less worrisome (6%). Endoscopy-specific distress (IES) was high in 14% of patients and higher than the distress related to the outcome. Anxiety scores in our study were increased compared to general population scores at all time points. Especially the fact that NS patients remained at increased levels one month after endoscopy makes the comparability of our scores with the population scores questionable [19]. General population scores are not available for procedure specific-distress (IES), as this can only be measured in patients. Considering the cut-off values for clinical scores, the prospect of endoscopy causes moderate distress.

The observation that patients under regular endoscopic surveillance may adapt to this invasive procedure should not result in an underestimation of the burden of regular endoscopic surveillance. The search for less invasive surveillance tests should continue, and frequency of surveillance should preferably be established by evidence-based individualized estimates of risk of progression.

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